UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Note to Reader
January 8, 1998

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply. EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, If unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues available in the information docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack E. Housenger, Acting Director
Special Review and Reregistration Division

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

October 23, 1998

MEMORANDUM

SUBJECT: **Pirimiphos-methyl**. (Chemical ID No. 108102/List B Reregistration Case No. 2535). HED Human Health Risk Assessment and Supporting Documentation for the Reregistration Eligibility Decision Document (RED). No MRID #. DP Barcode Nos. D240741 and D241203.

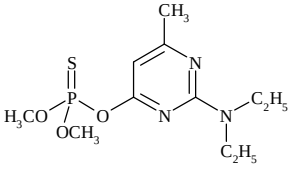
FROM: Christina B. Swartz, Chemist
Reregistration Branch 1
Health Effects Division (7509C)

THRU: Whang Phang, Ph.D., Branch Senior Scientist
Reregistration Branch 1
Health Effects Division (7509C)

TO: Dennis Deziel/Mark Wilhite (PM-51)
Accelerated Reregistration Branch
Special Review and Reregistration Division (7508W)

BACKGROUND

Pirimiphos-methyl [O-(2-diethylamino-6-methyl-pyrimidinyl) O,O-dimethyl phosphorothioate] is an organophosphate (OP) insecticide belonging to the phosphorothioate subclass of organophosphates. Similar to other OPs, pirimiphos-methyl inhibits important nervous system enzymes known as cholinesterases (ChE). Pirimiphos-methyl is marketed for occupational uses only, including post-harvest control of many types of pests on stored grains/seed and fly control on livestock. Under a special local needs (SLN) registration, pirimiphos-methyl is used to control mealy bugs on iris bulbs via fumigation in a single propagation nursery in Washington State.



Pirimiphos-methyl

Products containing pirimiphos-methyl are formulated into liquid concentrates, ready-to-use solutions and treated articles (ear tags). Based on uses supported through reregistration, human

health risk is associated with potential exposure to pirimiphos-methyl through consumption of treated crops and livestock commodities, and in occupational settings. The HED Metabolism Assessment Review Committee (MARC) has determined that the residues of concern in stored grain and livestock commodities include pirimiphos-methyl and its des-ethyl metabolite. However, in order to harmonize with CODEX, only the parent, pirimiphos-methyl, is included in the revised tolerance expression [40 CFR §180.409]. Dietary exposure to both the parent and the des-ethyl metabolite has been included in dietary risk assessments conducted for pirimiphos-methyl.

In conjunction with preparation of the human health risk assessment for pirimiphos-methyl, HED scientists have completed the following:

Report of the Hazard Identification Assessment Review Committee: Jess Rowland, 1/29/98;
The ORE aspects of the HED Chapter of the RED: Jeff Dawson, 4/9/98;
Toxicology Chapter of the Reregistration Eligibility Document: Sanju Diwan, Ph.D., 5/15/98;
Conclusions of the Metabolism Assessment Review Committee: Jerry Stokes, 5/15/98;
Product and Residue Chemistry Chapters of the HED RED: Christina Swartz, 6/1/98; and
Acute and Chronic Dietary Risk Analyses: Christina Swartz, 7/21/98.

In a report dated 1/29/98, the HED Hazard Identification Assessment Review Committee (HIARC) evaluated the toxicology database for pirimiphos-methyl and selected doses and endpoints for acute and chronic dietary risk assessments, and for occupational risk assessment (based on registered use patterns, residential exposure to pirimiphos-methyl is not expected to occur). The Committee also addressed the sensitivity of infants and children, as required by the Food Quality Protection Act (FQPA) of 1996. In meetings conducted to assess consistency in selecting endpoints and safety factors for all organophosphates, changes were made to the conclusions of the HIARC (refer to the summary documents “Hazard Assessment of the Organophosphates: Report of the HIARC”, J. Rowland, 7/7/98 and “FQPA Safety Factor Recommendations for the Organophosphates,” B. Tarplee, 8/6/98). The recommended changes have been incorporated into the discussion of the toxicology database presented herein. The current conclusions with respect to dietary and occupational risk reflect the changes in HIARC and FQPA Factor Recommendations, even though these changes have not been incorporated into the individual RED chapters.

Supporting documents refer to the NOEL (no observed effect level) and LOEL (lowest observed effect level) in toxicology studies. In order to harmonize with other offices in EPA, and to express greater clarity in scientific decision-making, OPP/HED has decided to use the terms no observed *adverse* effect level (NOAEL) and lowest observed *adverse* effect level (LOAEL) [policy memorandum, M. Stasikowski, 9/22/98]. The new policy is reflected in the current risk assessment.

SUMMARY/CONCLUSIONS

Available data indicate acute and chronic dietary risk associated with exposure to pirimiphos-methyl exceeds the Agency's level of concern for the general U.S. population and for population subgroups including infants and children (1-6 years and 7-12 years). Both acute and chronic dietary risk assessments were based on highly refined residue data (see Table 3). Data pertaining to the potential for concentration/reduction of residues in high fructose corn syrup could be used to further refine the Agency's dietary risk assessments. In addition, submission of required toxicology data to remove the 10X uncertainty factor (for chronic assessments only) for toxicology data gaps could alleviate the Agency's concerns for chronic dietary risk (refer to the detailed considerations). A probabilistic assessment of acute dietary exposure to pirimiphos-methyl was not conducted by the Agency, but could further refine acute dietary risk. An aggregate exposure/risk assessment (i.e., including residential exposure and dietary exposure through drinking water) is not applicable, based on registered use patterns for pirimiphos-methyl.

Data summarized in a 10/97 report, "Evaluation of Pirimiphos-methyl: Evaluation of Use in Agriculture, Horticulture, Food Storage Practice and Home Gardens," completed by the UK Ministry of Agriculture, Fisheries and Food (MAFF), indicate there is likely to be some dietary risk associated with imported commodities treated with pirimiphos-methyl. Although the UK monitoring data are not adequate to quantify dietary risk using from imported commodities, the data suggest that residues in imported commodities are generally low or below the limit of detection. Dietary risk from imported commodities has not been included in the human health risk assessment completed by HED.

Intermediate-term occupational exposure and concomitant risk associated with mixing, loading and applying products containing pirimiphos-methyl for bin disinfestation and top-dress treatments exceeds the Agency's level of concern. Due to a lack of chemical-specific data, occupational exposure/risk assessment for handlers was accomplished using surrogate data of varying quality from the Pesticide Handlers Exposure Database (PHED, 5/97 Surrogate Data Table), label information (i.e., for iris bulb fogging) and cultural practices information.

The unacceptable MOEs for intermediate-term exposure represent the maximum level of mitigation through additional PPE and engineering controls currently applied in HED. Intermediate-term occupational risk for handlers could be refined via submission of additional information such as typical application rates, the amount of grain handled, data pertaining to dermal absorption, and chemical- or scenario-specific data.

DATA REQUIREMENTS

Additional data requirements have been identified in the science chapters (see attachments).

Toxicology:

The following studies must be submitted (OPPTS Test Guideline Nos. indicated in parentheses):

Acute delayed neurotoxicity study in hens (870.6100);
Chronic toxicity study in dogs (870.4100); and
Combined chronic toxicity/carcinogenicity study in rats (870.4300).

Product and Residue Chemistry:

Registered labels should be amended to remove the uses on rice and wheat "for export only." The use on bulk/bagged seed should be removed from registered labels pending satisfaction of OPPTS 860.1500 (see below). Note that HED has recommended a revision in the tolerance expression to include only residues of the parent pirimiphos-methyl *per se*. Data are required as follows:

OPPTS Guideline No. 830.7050: UV/Visible absorption data;
OPPTS Guideline No. 860.1380: Storage stability data to support residue trials on grain; and
OPPTS Guideline No. 860.1500: Magnitude of the residue in forage/stover grown from treated bulk/bagged seed.

Occupational Exposure:

Label language referring to personal protective equipment (PPE) and engineering control use must be altered to reflect the basis of the current occupational exposure/risk assessment. For example, for admixture and bulk/bagged seed treatments, the HED assessment is based solely on the use of closed systems; labels must be revised to prohibit use of open systems. For the fogging use on iris bulbs in Washington State, the label must be amended to reflect concerns over entry into previously fogged areas and to require glove use at planting. Site-specific incident data and health and safety programs of the company that makes the applications should be provided for the iris bulb fogging use. For scenarios which exceed HED's level of concern for intermediate-term risk, additional mitigation measures are required.

Scenario-specific exposure data and additional cultural practices information could be used to refine the Agency's risk assessment for occupational handlers.

DETAILED CONSIDERATIONS

TOXICOLOGY

The toxicology database for pirimiphos-methyl is not complete, but can be used for human health risk assessments. The available toxicology data confirm the anticholinesterase activity of pirimiphos-methyl in various species, including humans, rabbits, guinea pigs, rats and mice. Pirimiphos-methyl causes dose-related inhibition in plasma, red blood cell (RBC) and brain cholinesterase (ChE) activity by all routes of exposure and following exposure for various durations. Clinical symptoms associated with exposure to pirimiphos-methyl include tremors, ataxia, leg paralysis, abnormal gait and salivation. However, none of the animal studies submitted to EPA indicate changes in brain weight or histopathology. Cholinesterase inhibition occurs at very low dose levels, and is recoverable when exposure is discontinued. Pirimiphos-methyl has relatively low acute oral, dermal and inhalation toxicity; both eye and skin irritation were observed in rabbits (Table 1).

Studies submitted to EPA indicate that younger rats are equally susceptible to ChE inhibition as older rats, and there appears to be no increase in sensitivity among fetuses or pups following pre- and/or post-natal exposure. However, the additional uncertainty factor required by FQPA was retained at 3X, since the data are not adequate to evaluate neurotoxicity following acute and long-term exposure, or to assess the functional development of young animals and in turn the susceptibility to infants and children. Insufficient data are available to assess the need for a developmental neurotoxicity study.

The HIARC concluded that the chronic/carcinogenicity studies submitted to EPA are not adequate to determine the carcinogenic potential of pirimiphos-methyl; however, acceptable mutagenicity studies indicate no genotoxicity concerns.

Table 1. Acute Toxicity Profile

OPPTS GDLN	MRID	Study Type	Species	Results	Tox Category
870.1100	00126257	Acute Oral	rat	LD_{50} = 2.4 g/kg	III
870.1200	00126257	Acute Dermal	rabbit	LD_{50} = >3.5 g/Kg for females and between 2.2-3.5 g/Kg for males	III
870.1300	41556304	Acute Inhalation	rat	LC_{50} = >4.7 mg/L	IV
870.2400	00126257	Primary Eye Irritation	rabbit	Irritant	II
870.2500	00126257	Primary Skin Irritation	rabbit	Moderate Irritant	III
870.2600	00126257	Dermal Sensitization	guinea pig	Non-sensitizer	N/A

N/A = Not applied; * With the exception of this study, all other acute toxicity studies were conducted on the 75% formulation of pirimiphos-methyl.

TOXICITY ENDPOINTS

The toxicological endpoints for risk assessment are summarized in Table 2 and discussed below.

Table 2. Toxicological Endpoints for Risk Assessment.[1]

EXPOSURE SCENARIO	NOAEL (mg/kg/day)	ENDPOINT	STUDY	UNCERTAINTY FACTORS[2]
Acute dietary aRfD = 0.0083 mg/kg/day	0.25	Plasma ChE (day 14) Inhibition	28-day Human 56-day Human	10X (Conventional) 3X (FQPA)
Chronic dietary RfD = 0.00025 mg/kg/day	0.25 (LOAEL)	Plasma ChE (day 14) Inhibition	56-day Human	10X (Conventional) 10X (Data gaps) 3X (lack of NOAEL) 3X (FQPA)
Short-/Intermediate-/Long-Term dermal [Occupational only]	0.25 (LOAEL for intermediate- and long-term)	Plasma ChE inhibition [100% dermal absorption assumed]	28-day Human (oral, short-term) 56-day Human (oral, intermediate- and long-term)	**Short-term** 10X (Conventional) **Intermediate- term** 10X (Conventional) 3X (lack of NOAEL) **Long-term** 10X (Conventional) 10X (Data gaps) 3X (lack of NOAEL)
Short-/Intermediate-/Long-Term inhalation [Occupational only]	0.25 (LOAEL for intermediate- and long-term)	Plasma ChE inhibition [100% inhalation absorption assumed]	28-day Human (oral, short-term) 56-day Human (oral, intermediate- and long-term)	

[1] NOAEL = No Observed Adverse Effect Level; LOAEL = Lowest Observed Adverse Effect Level; ChE = Cholinesterase.

[2] Since endpoints for risk assessment were selected from human studies, the conventional uncertainty factor of 10X is applied to account for intra-species variability. Other uncertainty factors are as noted.

Acute Dietary Endpoint for Risk Assessment

The acute dietary endpoint was selected from 28-day (5 male test subjects) and 56-day (3 male subjects, 4 female subjects) oral human studies in which the only dose tested was 0.25 mg/kg/day. In the 28-day study, no plasma or erythrocyte ChE was observed during days 1 through 7. In the 56-day study, statistically significant plasma ChE inhibition was observed in 3 females between days 14 and 35. Based on a lack of ChE inhibition up to day 7, the no observed adverse effects level (NOAEL) for acute effects was 0.25 mg/kg/day. An uncertainty factor (UF) of 30 is applied in assessing acute dietary risk [a factor of 10X for intra-species variability, and a factor of 3X as required under FQPA]. The acute dietary reference dose (aRfD), when adjusted to include the

FQPA factor, is the NOAEL/UF, or 0.0083 mg/kg/day.

Chronic Dietary Endpoint for Risk Assessment (Reference Dose, or RfD)

The reference dose (RfD) used in the chronic dietary risk assessment was obtained from a 56-day (3 male subjects, 4 female subjects) oral human study in which the only dose tested was 0.25 mg/kg/day. This dose was considered to be a lowest observed adverse effects level (LOAEL) for chronic effects since plasma cholinesterase inhibition was observed between days 14 and 35. Based on a LOAEL of 0.25 mg/kg/day, and applying an uncertainty factor of 1000 [10X for intra-species variability, 10X for chronic toxicity data gaps, 3X for lack of a NOAEL, and 3 as required under FQPA], the reference dose (RfD) is the LOAEL/UF, or 0.00025 mg/kg/day.

Dermal and Inhalation Endpoints for Occupational Risk Assessment

The occupational dermal and inhalation exposure endpoints were selected from the 28-day and 56-day oral human studies described above, in which the only dose tested was 0.25 mg/kg/day. Since endpoints were selected from oral studies, dermal and inhalation absorption rates, both assumed to be 100%, are applied to dermal and inhalation exposures in assessing risk associated with these exposures. Comparison of the acute oral and acute dermal LD_{50} from studies conducted in rats and rabbits indicate that the assumption of 100% dermal absorption (relative to oral absorption) is not likely to be conservative.

Short-term dermal and inhalation exposure

For short-term occupational exposure, the NOAEL of 0.25 mg/kg/day was selected from the 28-day study. The margin of exposure (MOE) uncertainty factor to account for intra-species variability in short-term occupational scenarios is 10.

Intermediate- and long-term dermal and inhalation exposure

For intermediate- and long-term occupational exposure, the LOAEL of 0.25 mg/kg/day was selected from the 56-day oral human study. The only dose tested was considered to be a LOAEL for chronic effects based on plasma cholinesterase inhibition in female subjects between days 14 and 35. For intermediate-term exposure scenarios, the margin of exposure uncertainty factor is 30, based on a factor of 10 for intra-species variability and a factor of 3 for lack of a true NOAEL. For long-term occupational exposure scenarios, the uncertainty factor is 300, including a factor of 10X for intra-species variability, a factor of 3X for the lack of a true NOAEL, and an additional factor of 10X for chronic toxicity data gaps.

AGGREGATE RISK

The FQPA of 1996 requires the Agency to consider aggregate exposure and concomitant risk in its decision-making process for dietary (food source and drinking water), residential, and other

non-occupational exposures. Since there are no residential exposure scenarios associated with registered uses of pirimiphos-methyl, and since no dietary exposure is expected through drinking water (L. Parsons memo dated 1/13/98), dietary risk is the only component of the aggregate risk assessment for the active ingredient pirimiphos-methyl.

DIETARY RISK

Acute and chronic dietary risk analyses were conducted using reassessed tolerances and anticipated residues described in the residue chemistry chapter. Although tolerances are reassessed to include residues of pirimiphos-methyl *per se*, dietary exposure and risk assessments include residues of the des-ethyl metabolite (refer to the MARC memo dated 5/15/98). Anticipated residues were calculated from field tests on stored grain. For chronic dietary exposure and risk assessment, these anticipated (average) residues were further refined using percent crop treated data (%CT) provided by BEAD, and subsequently modified as result of the high percentage of detects in FDA monitoring data, 1992-1996. Percent crop treated for grains was estimated to be <1% by BEAD, but up to 40% of the corn commodity samples analyzed by FDA contained detectable residues. BEAD scientists suggested that food corn may be more likely to treated than feed corn; furthermore, treated grain may be blended with untreated grain, resulting in a higher number of monitored samples with detectable residues. Subsequently, BEAD modified the estimated percent crop treated to include only corn grain grown for food, at 14 %CT [the number of samples analyzed by FDA was not sufficient to allow calculation of anticipated residues from monitoring data]. Since grains are blended, the average residues calculated from field tests served as the basis for non-probabilistic acute dietary risk assessments; in accordance with Agency policy, these residues were not adjusted for %CT.

Acute and chronic dietary risk analyses were conducted using the Dietary Exposure Evaluation Model (DEEM™). The DEEM™ software estimates dietary exposure to pesticides in foods based on the 3-day average of consumption data collected in USDA's Continuing Surveys of Food Intake by Individuals, 1989-1992. Dietary risk is expressed as a function of dose through dietary exposure. Although all available data have been used to refine the dietary exposure estimates, both acute and chronic dietary risk exceed the Agency's level of concern for the general U.S. population and population subgroups including nursing (acute only) and non-nursing infants, children 1-6 and children 1-12. If the required toxicology studies are submitted, and the 10X uncertainty factor for data gaps is removed, then chronic dietary risk could fall below the Agency's level of concern. Dietary risk is summarized in Table 3.

Table 3. Summary of Dietary Risk for Pirimiphos-methyl.

Population Subgroup	Acute Dietary Risk (% acute RfD)			Chronic Dietary Risk (% chronic RfD)
	95th %-ile	99th %-ile	99.9th %-ile	
U.S. Pop - 48 states - all seasons	143	247	429	226
Nursing infants (<1 year)	87	108	112	87
Non-nursing infants (<1 year)	266	510	1740	353
Children (1-6 years)	272	399	628	505
Children (7-12 years)	198	294	490	390

Examination of a commodity contribution analysis for chronic dietary risk indicates most of the chronic dietary risk for pirimiphos-methyl is due to consumption of high fructose corn syrup (HFCS). Since there are no data on the potential for concentration or reduction of pirimiphos-methyl residues during processing of corn grain into HFCS, the anticipated residue in corn grain was used for HFCS in the analysis. A processing study depicting the potential for concentration in HFCS could further refine the Agency's risk assessment.

A 10/97 study entitled "Evaluation of Pirimiphos-methyl: Evaluation of Use in Agriculture, Horticulture, Food Storage Practice and Home Gardens," completed by the UK Ministry of Agriculture, Fisheries and Food (MAFF) was submitted to EPA [no MRID #, DP Barcode No. D241203]. The study report summarizes use patterns and residue data for commodities grown outside the US. The uses covered include applications to apples (France, UK); plums, strawberries, black currants, carrots, onions, peppers, cauliflower, peas (seeds and whole pods), green beans, celery, potatoes and raspberries (UK); tomatoes (West Germany, UK and Holland); cucumbers, cabbages and lettuce (West Germany and UK); and Brussels sprouts (UK and Holland).

Conclusions of the MAFF regarding the nature and magnitude of the residue in stored grain are in general agreement with the conclusions summarized in HED documents. MAFF has followed the Codex policy of including only residues of pirimiphos-methyl *per se* in risk assessments. Metabolism data summarized in the MAFF report indicate that the des-ethyl metabolite comprises a maximum of 10% of the residue in treated crops. Average residues in the commodities listed above, based on field trial studies conducted in the countries listed, were summarized in the MAFF report. For most commodities, average residues ranged from a minimum of non-detectable (<0.01 ppm) to < 1 ppm. However, residues of up to 2 and 8 ppm were reported in Brussels sprouts and celery, respectively. There were no data available to assess registered uses on mushroom, broccoli, calabrese and wheat, and on pears grown in Northern Europe. The allowable daily intake (ADI) reported in the MAFF document is 0.03 mg/kg/day, taken from a

human study in which cholinesterase inhibition was selected as the endpoint; the report did not indicate if the ADI is for acute or chronic exposures in the diet.

Monitoring data generated by the UK Working Party on Pesticide Residues (WPPR) were also summarized in the MAFF report. In general, less than 100 samples were taken for each commodity; both imported (to the UK from other countries) and UK-grown commodities were sampled. The commodities included aubergine (eggplant); carrot; chili peppers; kiwi fruit; orange; sweet pepper; bran; biscuits; white rice (short and long grain); brown rice (long grain); buckwheat; millet; rye; bread crumbs; bread (wholemeal, white, multi grain, and brown); "organic" bread (wholemeal, brown, and white); malt extract (with and without fish oil); beef; lamb; cattle, sheep and pig kidney fat; and evening primrose oil.

Pirimiphos-methyl residues were detected in 7/23 kiwi samples (0.05-0.3 ppm); 2/91 orange samples (0.07, 0.1 ppm); 1/15 sweet pepper samples (0.2 ppm); 30/46 bran samples (0.05-0.6 ppm); 14/183 biscuit samples (0.05-0.1 ppm); 1/105 rice samples (0.05 ppm); 1/12 bread crumb samples (0.05 ppm); 2/37 wholemeal bread samples (0.07, 0.1 ppm); 1/25 brown bread samples (0.06 ppm); 1/37 white bread samples (0.06 ppm); 2/33 multi grain bread samples (0.05 ppm); 1/8 "organic" brown bread samples (0.08 ppm); and 1/4 samples of malt extract, without fish oil samples (0.07 ppm). Other commodities sampled, including all the livestock commodities, had no residues detected (<0.05 ppm).

Due to concerns regarding the potential for higher residues in single serving carrots, the MAFF limited the maximum number of applications to carrots, and continued to monitor residues in both composite and single serving samples of carrots. Reductions in the residues detected were observed, but the MAFF determined that "some erosion of safety margins for consumers still existed." Therefore, the restriction on the maximum number of applications to carrots has been retained, and the WPPR continues to monitor residues in carrots.

The UK report suggests that there is likely to be some dietary risk associated with pirimiphos-methyl uses in other countries. It is not possible to quantify the risk using the available information; however, the UK monitoring data suggest that residues are generally low or near the limit of detection.

OCCUPATIONAL RISK

Examination of use patterns on registered labels (i.e. no residential uses) indicates exposure is expected to occur in the course of typical activities for occupational workers; exposure assessments have been completed for occupational handler and post-application scenarios. Short-term and intermediate-term occupational exposure assessments were conducted, but chronic occupational exposure scenarios are not expected to occur, based on use patterns supported through reregistration.

For occupational handlers, six scenarios served as the basis for the exposure/risk assessment. The registrant intends to propose a pour-on treatment for livestock (scenarios 4a and 4b in the ORE Chapter). The pour-on use was incorporated into the assessment dated 4/9/98, but is not included in the HED risk assessment for reregistration since it is not a registered use, and since it has not formally been submitted to the Agency. The potential for post-application exposure is expected only in conjunction with the fogging use on iris bulbs in Washington State; short-term inhalation exposure is of concern after greenhouse fogging operations. No other scenarios are expected to result in either dermal or inhalation post-application exposure.

Since there were no chemical-specific exposure or residue dissipation data, unit exposures (dermal and inhalation) for occupational handler scenarios were derived from the Pesticide Handlers Exposure Database (PHED Surrogate Data Table, 5/97); several handler assessments were completed using "low quality" PHED data due to the lack of higher quality data. No surrogate data were available to assess exposure during application of ear tags to livestock. Several generic protection factors were used to calculate handler exposures, although protection factors for clothing layers have not been completely evaluated by HED. In calculating daily exposures, factors such as tons of grain treated per day were based on best professional judgement due to a lack of pertinent data. Empirical data were not available for determining post-application inhalation exposure after greenhouse fogging, and therefore air exchange rates and anticipated chemical dissipation patterns were used to derive an exposure concentration for pirimiphos-methyl.

For short-term exposure, a margin of exposure (MOE) of 10 is considered to be protective, while an MOE of 30 is considered protective for intermediate-term occupational exposure. A summary of occupational scenarios and associated risks assuming the baseline clothing scenario, protective clothing and PPE (personal protective equipment), and engineering controls is presented in Table 4. Shaded regions in the table indicate scenarios for which occupational exposure exceeds the Agency's level of concern for short-term and intermediate-term risk. HED notes that for some scenarios with unacceptable MOEs (mixing/loading/applying for bin disinfestation or topdress treatment), further mitigation of risk using engineering controls is not feasible, due to the type of equipment involved. These scenarios include applications using either a high pressure hand-wand or backpack sprayer, for which engineering controls typically do not exist.

HED is particularly concerned with the potential for intermediate-term risk to occupational workers mixing, loading and applying products containing pirimiphos-methyl for bin disinfestation and top-dress treatment. The MOEs are unacceptable, even though protection factors were applied to adjust exposure for additional clothing (personal protective equipment, PPE). Although short-term risk exceeds the Agency's level of concern at the maximum level of mitigation (MOE = 9, whereas an MOE of 10 is considered to be protective), HED notes that in the oral human study selected for short-term risk assessment, the endpoint was a *lack* of cholinesterase inhibition up to day 7. Therefore, HED is not concerned about short-term occupational exposure and risk for pirimiphos-methyl, provided additional protective clothing is used, and provided application instructions on registered labels are followed.

Table 4. Summary of Occupational Risk for Pirimiphos-methyl.[1]

Exposure Scenario	Baseline Clothing[2]		Protective Clothing/PPE[3]		Engineering Controls[4]	
	Short-Term Risk (MOE)	Intermediate-Term Risk (MOE)	Short-Term Risk (MOE)	Intermediate-Term Risk (MOE)	Short-Term Risk (MOE)	Intermediate-Term Risk (MOE)
Mixer/Loaders						
Mixing/loading Liquids For Admixture Grain Treatment	N/F	N/F	N/F	N/F	300 (min rate) 230 (max rate)	300 (min rate) 230 (max rate)
Mixing/loading Liquids For Seed Treatment	N/F	N/F	N/F	N/F	1100	1100
Loading Liquids For Fogging Treatment of Iris Bulbs	<1	<1	35	35	N/F	N/F
Applicators						
Fogging Treatment of Iris Bulbs	12	N/A	12	N/A	N/F	N/A
Cattle Ear Tags	No Data	No Data	No Data	No Data	N/F	N/F
Mixer/Loader/Applicator						
Mixing/loading and Applying Liquids Using a Low Pressure Handwand [Top dress]	<1	<1	69	69	N/F	N/F
Mixing/loading and Applying Liquids Using a Low Pressure Handwand [Bin Disinfestation]	<1	<1	38	38		
Mixing/loading and Applying Liquids Using a Backpack Sprayer [Top dress]	10	10	16	16	N/F	N/F
Mixing/loading and Applying Liquids Using a Backpack Sprayer [Bin Disinfestation]	5	5	9	9		
Mixing/loading and Applying Liquids Using a High Pressure Handwand [Top dress]	10	10	16	16	N/F	N/F
Mixing/loading and Applying Liquids Using a High Pressure Handwand [Bin Disinfestation]	5	5	9	9		

[1] Only occupational risk is summarized, since there are no residential exposure patterns based on the registered uses. The data are summarized from the 4/9/98 ORE Chapter of the HED RED.

N/A = not applicable; N/F = Not Feasible (the assumption of either baseline clothing, additional PPE or engineering controls does not exist for the relevant scenario).

MOE = Margin of Exposure = NOAEL (or LOAEL)/exposure; MOEs of 10 and 30 are considered to be protective for short-term and intermediate-term occupational exposures, respectively.

[2] The baseline clothing and PPE scenario consists of workers wearing a single layer of clothing, no gloves, and no respirator. Mixing/loading activities are open; open cab is assumed for applicators and flaggers.

[3] Additional PPE scenarios consist of workers wearing a double layer of clothing, chemical resistant gloves and a respirator.

[4] For engineering controls scenarios, it is assumed that workers wear a single layer of clothing and no gloves while using an appropriate engineering control system (i.e., closed mixing, enclosed cabs).